Talanta Open 11 (2025) 100432

Contents lists available at ScienceDirect

Talanta Open

journal homepage: www.sciencedirect.com/journal/talanta-open

MIP-based sensing strategies for the diagnosis of prostate and lung cancers

İnci Uludağ Anıl, Mustafa Kemal Sezgintürk *

Faculty of Engineering, Bioengineering Department, Çanakkale Onsekiz Mart University, Çanakkale, Türkiye

ARTICLE INFO

Keywords:
Molecularly imprinted polymers
Lung cancer
Prostate cancer
Biosensor

ABSTRACT

Prostate and lung cancer are among the most prevalent and lethal forms of the disease, and, globally, cancer is a primary cause of mortality. Early diagnosis and the application of precise biomarkers are crucial for prolonging patient lifespan and enhancing quality of life. Molecularly imprinted polymers (MIPs) are synthetic substances capable of selectively identifying and binding specific target molecules. Besides their sensitivity to biomolecules, MIPs offer significant advantages in cancer biomarker detection due to their cost-effectiveness and flexible architectures. MIP-based biosensors designed for the detection of prostate and lung cancer-specific biomarkers provide unique solutions that enhance the diagnostic process and improve its accuracy. This study aims to assess the present state of MIP-based biosensors in the detection of biomarkers for prostate and lung cancer, as well as the potential opportunities provided by this technology. This study will present an overview of potential biomarkers for lung and prostate cancer, clarify the fundamental features of MIPs, and discuss their uses in MIP-based biosensors along with prospective future applications. In this context, our review is aimed to contribute to the development of innovative methods used in early cancer diagnosis.

1. Introduction

Cancer is a prevalent type of disorders characterised by unregulated proliferation of cells and their spread to other healthy areas of the body. In 2020, there were an estimated 19.3 million new cancer diagnoses and nearly 10.0 million cancer fatalities globally. Lung cancer is the second most prevalent cancer in women, following breast cancer, and the most prevalent cancer in males, followed by prostate and colorectal cancer regarding incidence. The statistics indicate that lung and prostate cancers represent a significant effect on world health [1]. The demand for cost-effective, dependable, and rapid technologies for early diagnosis of prostate and lung cancer is on the rise, as they are among the most prevalent and lethal forms of cancer worldwide. The early detection of cancer is crucial in the battle against the disease, as it enables the disease to be detected at a treatable stage. This enhances the survival rate of patients by enhancing the response to treatment and simplifying disease management as a result of cancer diagnosis in its early stages. In addition, the quality of life of patients is enhanced by the reduction of treatment-related complications and adverse effects, which is facilitated by the use of less invasive treatment methods as a result of early diagnosis. Innovative methods, particularly those that are facilitated by the precise identification of cancer biomarkers, enhance the efficacy and accessibility of early diagnosis processes.

Synthetic polymers known as MIPs are intended for the selective identification of biomolecules and low molecular weight targets. They possess significant potential in biosensor technologies, particularly in the early diagnosis and management of fatal diseases like cancer, as a result of these properties [2]. MIP-based biosensors are a unique and innovative approach to the detection of markers associated with these cancer types. This is due to the fact that their structures are designed to resemble natural biomolecules, which allows for high selectivity and stability. Furthermore, they have the capacity to enhance the sensitivity of biosensor platforms and circumvent certain constraints of conventional methods. MIPs are more economical than biomolecules and provide an alternative to biological recognition components like enzymes or antibodies [3]. Moreover, they enhance biosensor efficacy owing to their elevated affinity and selective binding capability to target molecules. However, the inability to completely remove the template molecule from the polymer, nonspecific binding, and complexity in the manufacturing process may negatively affect sensor sensitivity and accuracy [4]. The successful immobilization of the MIP on the electrode surface, optimization of binding kinetics, and efficient removal of the template molecule without compromising sensor performance are essential factors.

Techniques for effective immobilization of MIP on electrode surfaces include several ways applied to generate artificial recognition sites on

* Corresponding author.
E-mail address: msezginturk@hotmail.com (M.K. Sezgintürk).

https://doi.org/10.1016/j.talo.2025.100432
Received 28 January 2025; Received in revised form 8 March 2025; Accepted 12 March 2025
Available online 13 March 2025

biosensor surfaces. Bulk imprinting, surface imprinting, and epitope imprinting are three main imprinting methods. Small molecules are imprinted mostly by bulk imprinting. The polymer dissolves to reveal the recognition sites following polymerization. Since surface imprinting forms the recognition sites on the surface and the binding kinetics are faster, it is more appropriate for imprinting biomolecules. Its sensitivity may be less than volumetric printing, nevertheless, given the modest number of recognition sites. Among surface printing processes are soft lithography, template immobilization, grafting, and emulsion polymerization. While template immobilization generates consistent imprinted surfaces with chemical bonds, soft lithography lets the generation of micro- and nano-patterns free from the requirement for costly equipment. While emulsion polymerization generates MIPs at the nano- and micro-scale, grafting provides improved control over polymer shape. Epitope imprinting lets a particular area of the protein imprint rather than the whole protein. This approach reduces non-specific binding while nevertheless allowing more precise and powerful interactions. Since it concentrates just on the main sequences of proteins, it also provides the possibility for protein capture depending on genetic information. When selecting among these procedures, one must consider the molecular size to be imprinted, the polymer's accessibility, and the specifications of the biosensor application [5,6].

This review discusses studies on the detection of biomarkers specific to lung and prostate cancer, the most prevalent cancer types, utilizing MIP-based biosensors, along with their advantages, limits, and prospective future uses.

2. Lung cancer detection strategies

Lung cancer is the predominant and primary cause of cancer-related mortality globally. Early diagnosis and intervention are essential for effective disease management and enhancing survival rates. MIP-based sensors represent a promising method for detecting lung cancer-specific biomarkers, owing to their exceptional selectivity, durability, and cost-effectiveness. Blood is a prominent initial option for potential biomarkers in lung cancer diagnosis. Blood-based biomarkers give a comprehensive assessment of the entire human organism, encompassing the primary tumor, metastatic illness, immune response, and peritumoral stroma [7]. In this context, the concentrations of several biomarkers are assessed for early cancer detection. Aberrant glycosylation is frequently linked to the onset and advancement of diseases, including cancer, inflammation, and some congenital disorders [8]. Therefore, numerous glycoproteins, including alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA), possess potential as typical cancer biomarkers. However, it has been indicated that CEA as a biomarker for lung cancer may possess predictive value, yet it lacks sufficient strength to advise treatment decisions [9]. The utilization of tumor marker indices, encompassing many tumor markers, to assess patient prognosis and recurrence risk may prove advantageous in the future management of lung cancer patients.

This part of the review will comprehensively investigate MIP-based sensors created for potential lung cancer detection biomarkers, categorized by measurement methodologies.

2.1. Electrochemical detection

Glutathione (GSH) is essential for detoxifying and eliminating carcinogens in healthy cells, serving as a vital element of the antioxidant system. Alterations in this system and disruptions in GSH homeostasis significantly contribute to tumor development, progression, and treatment response. GSH, typically present in elevated concentrations within tumor cells, has been linked to tumor advancement and chemotherapeutic drug resistance [10]. Moreover, tumor cells maintain increased nicotinamide adenine dinucleotide (NADPH) levels relative to healthy cells to enhance their redox defenses and facilitate biosynthetic processes [11]. The initial phase of cancer is attributed to cellular dysfunctions linked to alterations in these reduction mechanisms. In lung cancer patients, the absolute value of GSH, NADPH and redox potentials were found to be significantly lower compared to healthy individuals, while glutathione disulfide (GSSG) levels were found to be significantly higher. The findings derived from blood tests suggest that GSH, NADPH, $NADP^{*}$, and Redox potentials (Ehc) levels may act as promising indicators for the early identification of lung cancer. Given that a solitary analyte yields restricted information, there is a significant necessity for a multiplex biosensor system to concurrently assess several redox species pairs, hence enhancing the investigation of overall redox homeostasis in cancer patients. Liu and colleagues developed a multiplex electrochemical biosensor system employing a MIP film on glassy carbon electrodes (GCE) for the amperometric quantification of GSSG, GSH, cysteine (Cys), cystine (Cyss), β-nicotinamide adenine dinucleotide phosphate ($NADP^{+}$), and NADPH in samples of blood from lung cancer patients and healthy donors. They utilized the "MIP-Gate effect" detection approach to concurrently study these compounds [12]. MIPs, the gate effect results from the modification of the faradaic activity of a redox probe caused by the presence of analyte molecules within the imprinted cavities. Several mechanisms of the gate effect in analyte measurement using molecular imprinting are feasible. The structural MIP film is modified through swelling or shrinkage resulting from analyte binding. These structural modifications either augment or reduce the diffusion rate of electrolyte ions and/or the redox probe within the film. A different possibility may emerge from the alteration in the charge state of the MIP film. Moreover, the electrical configuration of the MIP may alter due to the doping of the MIP with the analyte, hence inducing the gate effect [13]. In comparison to analogous research, the proposed sensor exhibited a lower detection limit, a straightforward manufacturing method, and a dynamic range of concentrations for six analytes between 10^{-11} and 10^{-8} mol L^{-1}, with a detection limit (LOD) of 20 pmol L^{-1}.

Carcinoembryonic antigen (CEA) is a glycoprotein involved in cell adhesion. Despite the controversial nature of CEA as a reliable marker for lung cancer [14,15], its cost-effectiveness, non-invasive nature, and absence of alternative dependable markers render CEA a compelling choice in lung cancer diagnostics. The elevated levels of CEA in patient serum are being assessed as a diagnostic instrument for various types of lung cancer. Multi-template molecularly imprinted polymers can create various recognition sites on a single polymeric substrate by concurrently employing two or more target molecules as templates. In contrast to single-template MIPs, it presents significant potential for concurrent identification, enrichment, and multiplex detection, hence expanding the applicability in real samples [16,17]. Wang et al. developed a signal amplification technique utilizing dual-template magnetic-MIPs with graphene-Au signal labels for the simultaneous detection of alpha-fetoprotein (AFP) and CEA. G–Au–rApo-M labels were employed for signal enhancement. A concentration of gold nanoparticles (AuNPs) on graphene offered several active sites for the conjugation of rApo and primary antibodies. The distinct reactivity of the inner and outer surfaces of apoferritin, along with its capacity to sequester small molecules within its protein cavity, presents prospects for the fabrication of multifunctional nanomaterials with regulated molecular characteristics. The selective capture probes were manufactured using the self-polymerization of dopamine on Fe_3O_4 nanoparticles (Fe_3O_4 NPs), utilizing AFP and CEA as a template molecules. The LOD for CEA and AFP were 0.35 and 0.3 pg mL^{-1}, respectively, which were inferior to earlier reported outcomes [18].

Taheri and colleagues developed an additional instance of a dual-template MIP (DMIP)-based sensing approach for the distinct detection of CEA and AFP as biomarkers for lung cancer. Utilizing nanostructured materials can enhance detection sensitivity in DMIP sensors. Electrochemical sensors utilize conductive polymer film-modified electrodes owing to their steady performance, excellent conductivity, and straightforward preparation. Polypyrrole (PPy) has garnered increasing interest owing to its facile electrochemical production, favorable redox

characteristics, elevated conductivity, and physical durability. Researchers employed the PPy- Methyl orange (MO) electropolymerization technique to synthesize a dual-template rectangular nanotube MIP on fluorine doped tin oxide (FTO) substrate. MO augmented the conductivity of polypyrrole (PPy), and MO-doped PPy (PPy-MO) facilitated the development of rectangular-shaped nanotubes. The favorable outcomes in quantifying AFP and CEA in human serum samples, along with the DMIP sensor's high sensitivity and stability, render it a potential technique for detecting AFP and CEA in serum samples [19]. Wang et al. developed a CEA-imprinted polymerized ionic liquid hydrogel film utilizing 1-benzyl-3-bromopropylimidazolium bromide (BCCPEimBr) ionic liquid as a functional monomer under mild conditions. The ionic liquid served as a functional monomer to synthesize hollow gold nanospheres (HGNBs) incorporated into molybdenum diselenide ($MoSe_2$) nanosheets. This study establishes that $MoSe_2$ is a prototypical semiconductor, wherein excitation by white light facilitates electron transfers from the band of valence to the band of conduction, leading to the formation of electron-hole pairs. Electrons may be transported to the electrode surface directly or through HGNBs to produce photocurrent. Fig. 1 illustrates the development process of the created biosensor. The results indicated that HGNBs significantly increase the photoelectrochemical reaction of $MoSe_2$ nanosheets. Under optimum circumstances, the LOD of the developed printed sensor was established at 11.2 pg mL^{-1}. The feasibility of the printed PEC sensor for quantifying CEA in actual clinical serum samples has also been proven [20].

2.2. Surface-enhanced Raman spectroscopy (SERS) based detection

Surface-enhanced Raman spectroscopy (SERS) is a potent vibrational measurements method that enables label-free, highly sensitive, and accurate characterization of the substances by the enhancement of localized electric fields at the surface of the plasmonic substance when stimulated by monochromatic light. This enhances the Raman scattering signal, facilitating the detection of low-concentration analytes and promoting the application of SERS as a diagnostic instrument for disease. SERS substrates comprise colloidal and monodisperse nanoparticles (NPs) exhibiting morphologies that vary from simple forms, including spheres, rods, and cubes, to intricate structures such as prisms, polyhedra, and other multidimensional materials. The improvement in SERS substrates results from the formation of "hot spots," which are junctions between two nanostructured elements where electric fields are intensified. The SERS phenomenon demonstrates significant distance dependence due to localized intense electric fields; consequently, the most intense SERS signals are achieved when the target analyte is within 2 nm of the substrate surface or when it adsorbs to the surface, with rapid decay occurring at greater distances [21]. Nonetheless, despite the sensitivity and potential of SERS-based investigations, they are constrained by some constraints. The signals from the Raman probe utilized in these research are situated in the fingerprint area (300–1800 cm^{-1}), making them susceptible to interference from Raman signals of endogenous proteins. Secondly, the intensity of the SERS peak employed for quantitative detection frequently exhibits unforeseen fluctuations attributable to variations in laser power and environmental conditions. Both aspects will influence the ultimate precision of quantitative detection and substantially restrict the further applicability of this technology for analyzing complicated biological materials. Lin et al. combined SERS and MIP technology for CEA detection, integrating two layers of core-shell nanoparticles onto the SERS substrate to achieve significant electromagnetic enhancement through the creation of numerous "hot spots". These "hot spots" may be located not just in the interstitial regions between core-shell nanospheres within the same layer however also across both the lower and upper layers of the nanospheres, leading to a substantial amplification of Raman signals. Furthermore, to prevent interference from signals of endogenous molecules, an alkynyl (C≡C) group with a triple bond (2024 cm^{-1}) was employed as a stable Raman probe for CEA detection in this investigation, utilizing the quiet area of Raman scattering. The biosensor achieved a detection limit of 0.064 pg mL^{-1} within the range of 0.1 pg mL^{-1} to 10 μg mL^{-1}. The efficacy of the engineered detection method has demonstrated significant potential for biomarker-driven cancer screening through the use of CEA detection in actual patient blood samples [22].

A peptide epitope and glycan are two structural components of a glycoprotein. The specificity of an immunoassay can be significantly enhanced if it simultaneously recognizes these two traits. Nevertheless, there have been limited research focusing on the concurrent identification of peptide epitopes and glycans of a target glycoprotein. Zhou et al. presented an innovative method called orthogonal dual MIP-based plasmonic immunosandwich analysis (odMIP-PISA), which utilizes dual-characteristic recognition to enhance specificity in the detection of

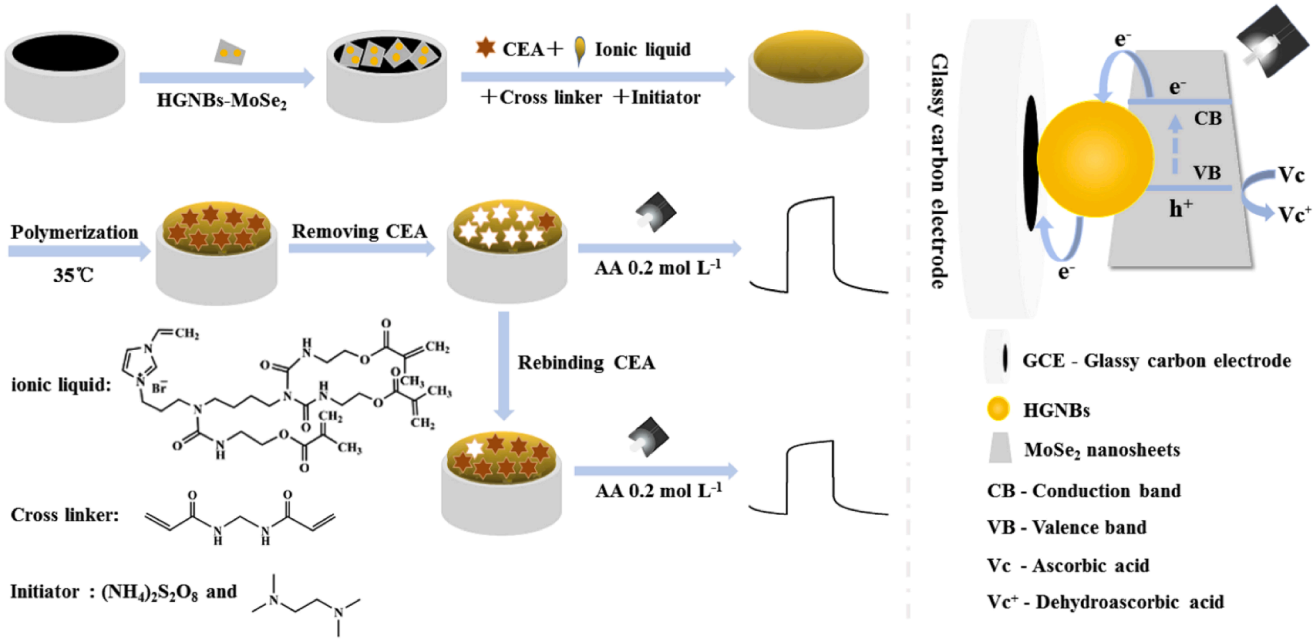

Fig. 1. Schematic representation of the manufacturing of CEA imprinted sensors and the PEC responses of HGNBs-MoSe2 nanocomposites [20].

glycoproteins. This strategy depends on the simultaneous detection of a target glycoprotein by two different types of MIPs, employing a surface covered with epitope-imprinted AuNPs as the capturing substrate for peptide epitopes and Raman-active nanoparticles of silver imprinted with glycans serve as marking nanotags for glycans. The unique properties of epitopes and glycans in the target molecule enable their recognition by two MIPs, creating an orthogonal pair of recognition features that is expected to promote a dual control mechanism and improve comprehensive recognition specificity in contrast to individual recognition. MIP thin layer specific to the C- or N-terminal epitope of the target glycoprotein was fabricated on a AuNP self-assembled monolayer (SAM) coated glass slide using the boronate affinity-assisted directed surface imprinting technique. The glycoproteins tagged with glycan-imprinted Raman nanotags created sandwich-like immunocomplexes on the glass slide, which was then analyzed by Raman detection. The epitope-imprinted AuNPs generated a hot spot in the interval between the SAM-coated slide and the Ag-core Raman nanotags, hence amplifying the SERS signals [23].

Previous approaches are anticipated to greatly impact forthcoming commercial point-of-care tools for protein identification, owing to their increased sensitivity and recognition capabilities; however, the nonspecific response from the component of biorecognition represents the principal limitation of these sensing strategies that requires resolution. Carneiro et al. presented a novel method that integrates two distinct biorecognition elements functioning collaboratively for the detection of CEA, hence minimizing nonspecific responses. This hybrid sandwich-like method employs a MIP film for sample pre-concentration on a solid substrate, alongside natural antibodies conjugated to metal nanoparticles that incorporate the Raman reporter as a transducer element. In this investigation, gallic acid (GA) was employed for the first time in the electropolymerization of a MIP film in the presence of CEA. The film was subsequently coated with a second ultrathin electropolymerized benzoic acid (BA) film to prevent nonspecific binding. GA possesses an aromatic ring with several hydroxyl groups, facilitating the formation of hydrogen bonds with the target template. Furthermore, it necessitates a low potential for oxidation and ensuing electropolymerization, signifying its role as an antioxidant. Gold nanostars (AuNSs) were favored as metallic substrates for SERS labeling. Raman reporter molecules must be affixed to the surface of AuNSs, and their interactions must be robust. Molecules featuring nitrogen or sulfur-containing functional groups are typically employed as Raman reporters because of their affinity for silver or gold nanoparticles utilized as SERS substrates. Four distinct Raman reporter molecules were evaluated, with 4-aminothiophenol (4-ATP) selected for its high signal intensity as the Raman reporter. The target molecule was detected at a concentration as low as 1 ng mL^{-1} using the antibody conjugated to the Raman reporter. The construction of the proposed biosensor is illustrated in the diagram in Fig. 2 [24].

Feng et al. propose an antibody-free immunoassay employing boronate affinity MIP and SERS tags. A boronate affinity array was developed by synthesizing a polymer that adsorbs glycoproteins onto a glass slide, employing 4-vinylbenzeneboronic acid (VPBA) as the functional monomer, ethylene glycol dimethacrylate (EGDMA) as the crosslinking agent, and ethylene glycol and cyclohexanol as porogens. A sandwich structure of a "MIP-target glycoprotein-SERS tag" was established through the covalent connection between the glycoprotein and the SERS nanotag, which comprises AuNPs and 4-mercaptophenylboronic acid (MPBA). The LOD for CEA attained a minimum of 0.1 ng mL^{-1} [25].

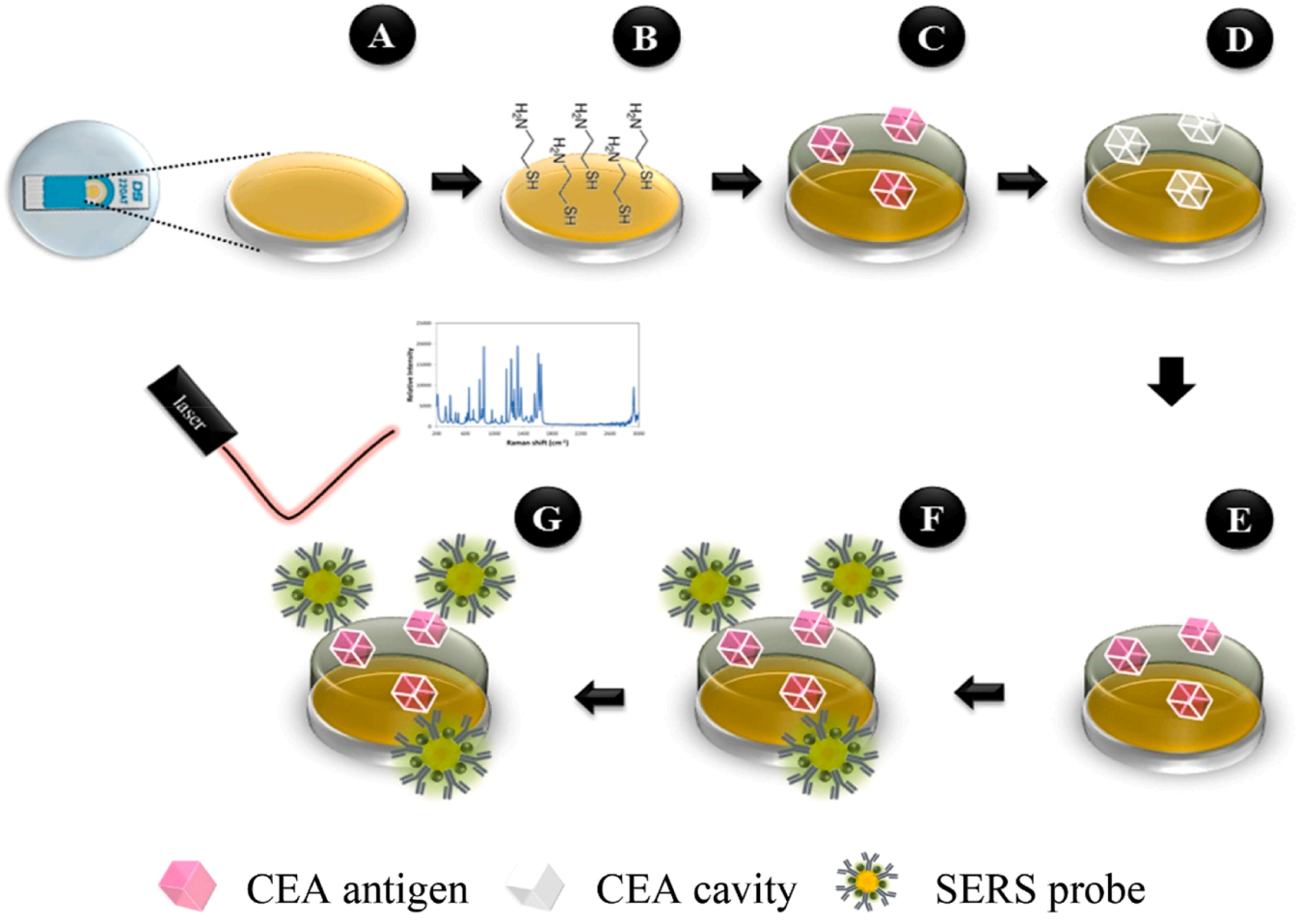

Fig. 2. Schematic representation of the biosensor assembly [24].

3. Prostate cancer detection strategies

Prostate cancer is among the most prevalent cancers in males and ranks as the second greatest cause of cancer-related mortality globally [1]. It is a condition that exhibits significant responsiveness to treatment when identified early. Biomarkers utilized in the diagnosis and monitoring of prostate cancer facilitate early intervention through precise and sensitive disease detection. The pathogenesis and advancement of prostate cancer are intricate and variable; active surveillance is favored for low-risk cases, whereas surgical intervention and radiotherapy are utilized for localized tumors. In metastatic or aggressive instances, combinations of hormone treatment, chemotherapy, radiation, and immunotherapy are employed. Consequently, the incorporation of clinically significant prognostic and predictive biomarkers is crucial for the prompt prevention of metastatic illness and the determination of therapy options. Prostate-specific antigen (PSA) is a protein mostly produced by cancerous prostate gland cells. Elevated PSA levels in the blood of men serve as a biomarker for prostate cancer or inflammation and tend to rise with age beyond 50 years. The PSA level is effective for tracking the progression and response of cancer patients following chemotherapy. On the other hand, some improvements have been made in PSA test to increase diagnostic accuracy against the risk of obtaining false positive results due to various factors affecting PSA levels [26]. In prostate cancer diagnosis, various biomarkers, in addition to PSA, also serve for early diagnosis.

This section of the review will thoroughly examine MIP-based sensors developed for possible biomarkers in prostate cancer diagnosis, classified by measurement techniques.

3.1. Electrochemical detection

Conductive polymers are utilized in the construction of sensor for the immobilization of diverse biological components, including enzymes, antigens, antibody receptors, and the synthesis of molecularly imprinted polymers. Conductive polymers provide excellent electrical conductivity and charge transfer capabilities. Consequently, a range of electrochemically and optically active conductive polymers are employed in the development of diverse sensors and biosensors as signal transduction mechanisms. Recently, numerous conductive polymers have been utilized in sensor design, with the most prevalent being polypyrrole (Ppy), polyaniline (PANI), polythiophene (PTH), and poly(3,4-ethylenedioxythiophene) (PEDOT) [27]. The copolymerization of several functional monomers is a novel strategy employed to enhance the efficacy of MIPs. The utilization of many functional monomers facilitates the establishment of various chemical interactions (e.g., hydrogen bonds, π-π interactions, electrostatic attractions) with the target molecule (template molecule). This facilitates enhanced recognition and binding of the template molecule. This technique enables the acquisition of polymeric structures exhibiting enhanced selectivity, sensitivity, and binding capacity [28]. Khumngern et al. created an electrochemical sensor, MIP/PEDOT:PSS@Fc/SPCE, by depositing a molecularly imprinted copolymer of o-phenylenediamine (o-PD) and o-aminophenol (o-AP), which was electropolymerized in the presence of PSA, onto a screen-printed carbon electrode (SPCE) that had been modified with a polystyrenesulfonate-doped poly(3,4-ethylenedioxythiophene) ferrocene composite (PEDOT:PSS@Fc). The imprinted copolymer, poly(o-PD-co-o-AP), functioned as an artificial antibody that captured PSA by hydrogen bonding and electrostatic interactions. PEDOT:PSS, a polymer exhibiting high electrical conductivity, encapsulated Fc, functioning as an electrochemical probe. PEDOT:PSS also enhanced the signal and stabilized Fc. The results indicated that these interactions produced a strong affinity between MIP and the target molecule. The dissociation value of 1.91×10^{-6} ng mL^{-1} signifies the development of a very effective and sensitive biosensor for PSA detection [29]. This sensor possesses significant potential for use in the early diagnosis of critical illnesses, including prostate cancer. Nonetheless, the efficacy in actual samples and long-term stability must also be assessed. The schematic representation of the biosensor fabrication process is illustrated in Fig. 3.

MIP film thickness is a critical factor that influences the recognition capability of MIP-based sensors. Electropolymerization conditions, including functional monomer concentration, potential cycle number, and potential scan rate, can be utilized to regulate film thickness. Yazdani et al. developed of a PSA nanobiosensor that is based on molecularly imprinted electrosynthesized polypyrrole (PPy). The electropolymerization of Py was examined in relation to potential cycle numbers in this study. The electrodes that were prepared using cycle numbers greater than five exhibited extremely low DPV signals, which were a consequence of the marker's low accessibility, which led to the formation of a thick PPy film. The nanobiosensor's binding isotherm was examined at various equilibrium concentrations of PSA using three distinct models: the Langmuir, Freundlich, and two-type simultaneous binging model. The Freundlich adsorption isotherm was employed to determine the optimal data fit, resulting in K and n values of 0.89 ng mL^{-1} and 10.93, respectively. The fact that the Freundlich model offers the most satisfactory fit is a clear indication that the nanobiosensor surface is heterogeneous and that the binding mechanism of PSA is influenced by this heterogeneity. The K value indicates that the binding of PSA to the sensor surface is not highly specific, but it is sufficiently effective. These models serve as a critical reference during the biosensor development process. Furthermore, the researchers evaluated the efficacy of nanobiosensors in clinical diagnosis by analyzing blood serum samples obtained from patients to determine the nanobiosensor's capacity to identify PSA in actual samples [30].

Myo expression has been markedly linked to steroid hormone signaling and hypoxia indicators in prostate cancer patients and has been assessed as a biomarker for early-stage diagnosis [31,32]. Karami et al. created a dual-modal impedimetric immunosensor utilizing an antibody-molecularly imprinted polymer to evaluate Myo serves as a marker expressed with PSA in prostate cancers. Initially, 3,3′-dithiodipropionic acid di(N-hydroxysuccinimide ester) (DSP) was self-assembled onto a gold screen-printed electrode (GSPE). Subsequently targeting proteins were via covalent bonds linked to DSP-GSPE. The MIP was generated on the SPE surface utilizing acrylamide as the functional monomer, N,N′-methylenebisacrylamide as the cross-linker, and PSA and Myo as templates, respectively. A nanocomposite (NCP) comprising multi-walled carbon nanotubes, graphene oxide, and magnetite nanoparticles decorated with PSA-specific antibodies (Ab) was produced and subsequently treated with MIP(PSA, Myo)-SPE. The Rct values of the generated immunocomplex were assessed following an immunological reaction between MIPs, PSA, and NCP. The disparity in the charge transfer resistance (R_{ct}) values of MIP(PSA, Myo)-SPE and NCP-MIP(PSA, Myo)-SPE implicitly suggested the PSA concentrations. The biosensor performance was evaluated in relation to the thickness of the MIP layer. Thereafter, the kinetic function of the SPR spectrometer was utilized to evaluate the binding affinity of MIP to an analytical samples and the interaction between PSA and NCP. The results demonstrated that the affinity of MIP to Myo was greater than that of PSA, and the affinity between PSA and NCP was greater than that of PSA and MIP [33]. The results indicate that Myo is anticipated to have a reduced limit of detection and enhanced sensitivity regarding detection performance. The researchers indicated that, despite the relatively low affinity of PSA, enough performance was attained by the optimization of binding kinetics. In future analogous research, given the robust interaction between PSA and NCP, it would be prudent to implement surface changes or blocking methods to enhance the biosensor's selectivity. Designs aimed at two target molecules necessitate meticulous design and optimization regarding affinities and kinetic constants. Fig. 4 schematically illustrates the assembly of the developed sensor and immunosensor. A separate investigation utilizing nanocomposites for PSA detection was carried out by Ma et al. [34]. In contrast to single-component nanomaterials, graphene nanoplatelet (GS)

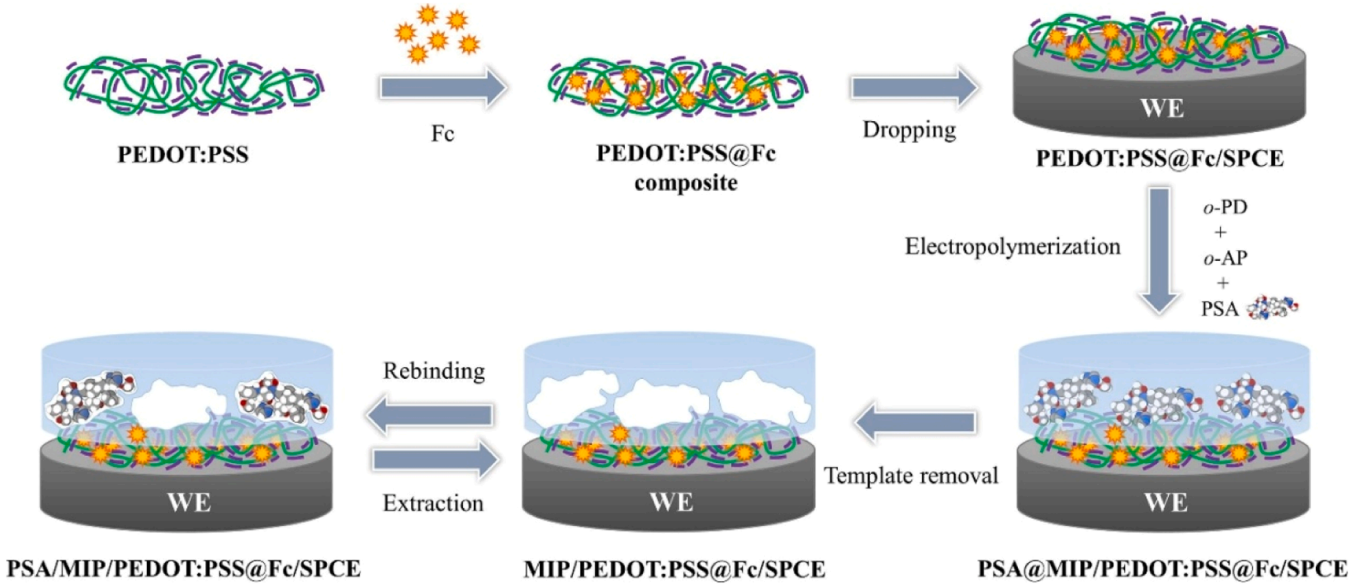

Fig. 3. Preparation procedure of MIP /PEDOT:PSS@Fc modified screen printing carbon electrode [29].

composites, particularly those incorporating coated metallic nanoparticles like Au, Ag, and Pt, exhibit superior particle dispersion and enhanced electrochemical characteristics owing to their synergistic effects [35]. Researchers designed of an amperometric sensor for PSA detection that integrates the benefits of a MIP with a nanocomposite of graphene nanoplatelets (GS), AuNPs, and chitosan (Chit). The sensitivity was markedly enhanced by employing the GS-AuNP hybrid signal. The designed sensor demonstrated a PSA levels range of 1 pg mL^{-1} to 100 ng mL^{-1} and a LOD of 0.15 pg mL^{-1} [34].

Ertürk et al. developed a microcontact imprinted (PSA-MIP) capacitive sensor that provides real-time, highly sensitive and specific measurement of PSA. Capacitive biosensors are a kind of electrochemical sensors that assess alterations in the dielectric characteristics of the sensor surface, that causes a reduction in capacitance following the contact between an analyte and the biorecognition element [36]. PSA-MIP electrodes were synthesized using UV polymerization utilizing methacrylic acid (MAA) as the functional monomer and ethylene glycol dimethacrylate (EGDMA) as the crosslinking agent. A microcontact printing technique was employed to apply PSA onto the surface of the capacitive sensor. Microcontact printing is a surface coating method employed to fabricate detection cavity for macromolecular mimics [37]. The target is attached to a glass substrate to create the protein imprint. It is then positioned in contact with the sensing layer. A thin polymer layer is created on the sensor surface using UV polymerization. The microcontact printing technique is an efficient approach that ensures great precision and uniformity on the surface during MIP manufacturing processes. This approach, however, has constraints including template molecule positioning, surface compatibility, and mold durability. This work involved the development of PSA-MIP and Anti-PSA electrodes to evaluate their detection performance and selectivity. The selectivity coefficients that for PSA and HSA indicated that the PSA-MIP electrode exhibited greater selectivity for PSA compared to the Anti-PSA electrode [36].

Abbasi et al. created an enhanced MIP-imprinted electrochemical analyses biosensor for PSA measurement. This study employed electrically conductive poly Toluidine Blue (PTB) as a synthetic receptor. The protein-imprinted PTB was electropolymerized within a preformed glutaraldehyde-cysteamine matrices on the gold electrode's surface. The researchers reported that the innovation of this study originated from using of TB as a functional monomer for the first time to fabrication of an electrically conductive MIP-based electrochemical sensor for PSA measurement. The MIP-modified electrodes exhibited a broad linear range of 1–60 μg L^{-1} and a lower limit of quantification (LLOQ) of 1 μg/L for PSA detection. The robust connection between the immunosensor findings and the results obtained through ELISA techniques confirmed the viability of the developed PSA immunosensor for the analysis of real biological samples [38].

MoS_2 is frequently used for enhancing sensing performance owing to its substantial surface area, superior electron transport characteristics, and chemical stability. Conductivity can be enhanced by incorporating conductive elements such as gold nanoparticles, carbon nanotubes, or graphene onto the MoS_2 surface. Effective surface modification techniques, utilization of suitable composites, and safeguarding against environmental influences can enhance the reliability and applicability of MoS_2-based systems. Zhang et al. devised a signal amplification approach in the biosensor they created for MIP-printed PSA detection. The signal was enhanced using the co-catalysis of AuNPs and MoS_2. The electrode surface was changed with MoS_2 and AuNPs as the sensing substrate. A PSA template and 4-mercaptophenylboronic acid (MPBA) were utilized to create MIP cavities, while MPBA-labeled gold polymerized methylene blue composites were developed as tracking labels. Target PSA is initially collected by the cavities by structural morphology, subsequently fixed onto the target sensor via the interaction between the cis-dihydroxy group of PSA within the cavities and MPBA. The MB signal from the tracking label, which is responsive to the concentration of target PSA due to the co-catalysis of AuNPs and MoS2 on the tracking label and substrate, exhibits a substantial amplification effect. The engineered sensor exhibited an extensive linear range from 1 $\times 10^{-4}$ to 1 $\times 10^{4}$ ng mL^{-1}, with a LOD of 0.03 pg mL^{-1} [39].

The MIP epitope imprinting technique aims to establish selective binding sites by utilizing a specific part of the target molecule (epitope) as a template, rather than the complete target molecule. This technique is mostly favored, particularly when focusing on large and intricate macromolecules (e.g., proteins, antigens). Epitopes enhance the identification of more precise areas for binding to the target molecule [40]. Shao et al. recently developed an epitope-imprinted electrochemical sensor for PSA measurement. This study initially described the use of The C-terminus region of PSA serves as a template molecule for the development of an epitope-MIP electrochemical sensor for determining PSA in actual serum. A MIP film targeting an epitope was generated on a gold electrode surface coated with AuNPs utilizing electropolymerization, employing the C-terminus region of PSA as a model and o-phenylenediamine as a functional monomer. AuNPs were incorporated to augment the surface area of the gold electrode, thereby

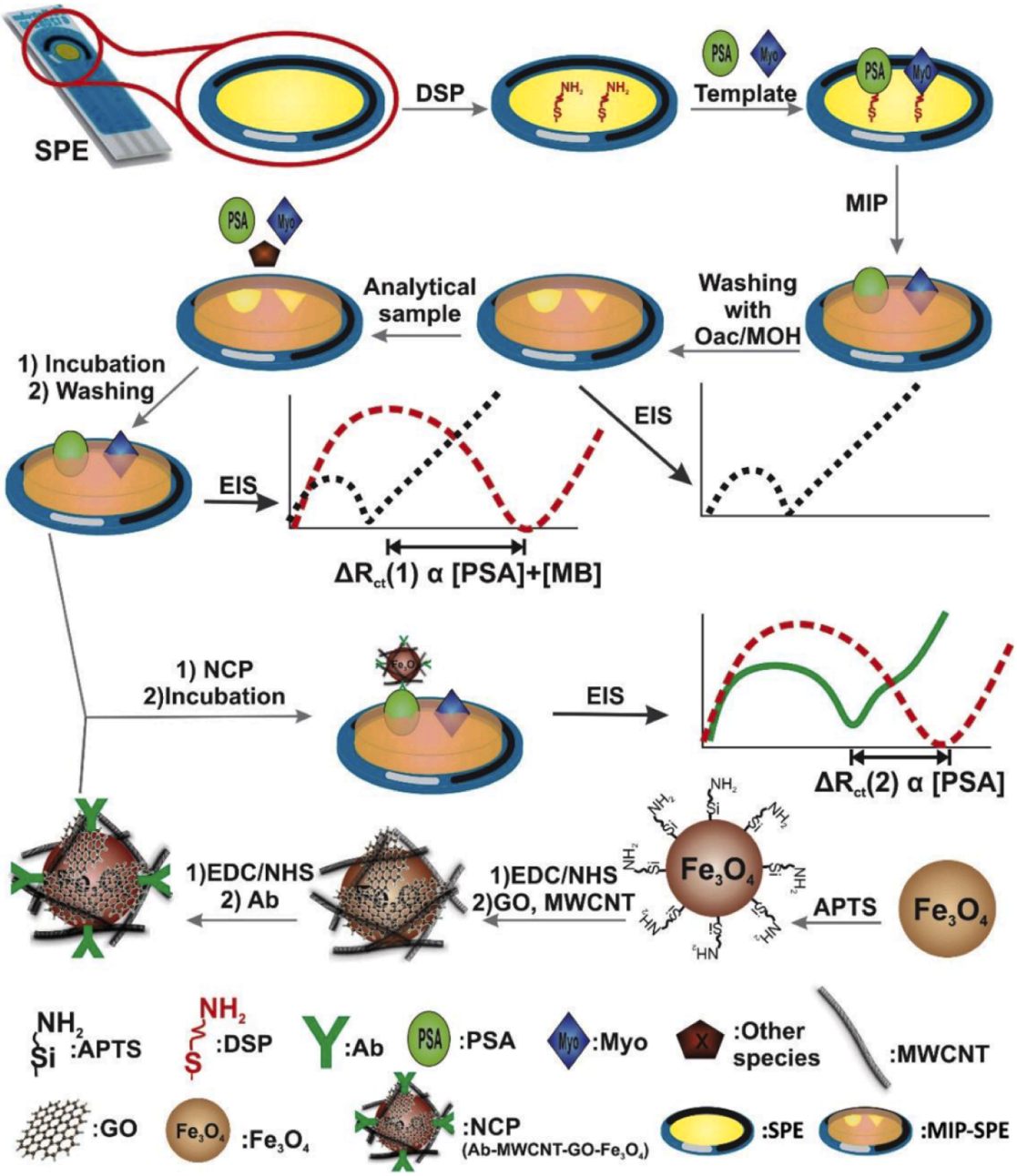

Fig. 4. Depiction of the construction and functionality of the designed immunosensor [33].

increasing the effective surface area for the immobilization of the epitope-MIP film. However, the researchers criticized the results, stating that the effective surface area (5.40×10^{-2} cm^2) was not high sufficient, that could affect the rapidly rebinding of PSA. Future studies will utilize other nanomaterials, like carbon nanotubes, graphene, and quantum dots, to address this issue. The sensor exhibited a very low LOD of 0.31 fg mL^{-1} over a wide various PSA concentrations from 1 fg mL^{-1} to 0.1 μg mL^{-1} [41]. The epitope imprinting technique provides considerable benefits, particularly in the creation of biosensors that necessitate the recognition and selective detection of biomolecules. While utilizing tiny templates offers cost and stability benefits, it is imperative to select the appropriate epitope and ensure specificity. This method is increasingly used in proteomics and clinical diagnosis to enhance the sensitivity and accuracy of biosensors.

Aptamers are favored over antibodies as template molecules for MIP due to their synthetic production, which eliminates risks of denaturation, degradation, or biological contamination. Aptamers exhibit significant chemical stability and can endure polymerization environments, including organic solvents and severe pH levels. Due of their diminutive dimensions, they can establish more precise and accessible binding sites inside the MIP matrix. These attributes enhance the target selectivity of MIP while mitigating the stability and production constraints encountered by antibodies [42]. Jolly et al. documented the development of an innovative synthesized receptor biosensor that integrates biomolecular detection components with molecular imprinting to minimize certain constraints of traditional protein imprinting. A thiolated DNA aptamer with specificity for PSA has been interacting with PSA before being immobilized on a gold electrode surface. The researchers suggested that regulated electropolymerization of dopamine coated the complex, thereby maintaining the aptamer in its binding conformation and enhancing its recognition capabilities [43].

Up to this point, PSA has been addressed as the most commonly used

marker for prostate cancer diagnosis. Nonetheless, the efficacy of PSA screening in diagnosing prostate cancer exhibits limited sensitivity, and PSA levels can be influenced by multiple factors, including age, prostatitis, urinary tract infections, and benign prostatic hyperplasia, resulting in unavoidable false-positive outcomes [44]. The absence of a reliable biomarker for prostate the significance of cancer detection and evaluation underscores the necessity for novel, specific, sensitive, and cost-effective biomarkers to optimize treatment strategies in the disease's early stages. A metabolomics study by Seekumar et al. [45] identified sarcosine (N-methylglycine) as a possible biomarker for prostate cancer in urine. Sarcosine, an intermediary in the production and breakdown of glycine, is significantly raised during the progression of prostate cancer to metastasis and is either undetectable or found at negligible quantities in the urine of healthy people. Fernández-Puig et al. employed MIP-based nanocomposite polymerized on silica nanoparticles to ascertain sarcosine in the creation of an all-solid-state (ASS) potentiometric sensor. Silica nanocomposites, serving as structural supports for MIPs, facilitated stable complexation of sarcosine and functional monomers. This research proposes the creation of the first potentiometric miniature ASS sensor for the detection of sarcosine [46]. Nguy et al. introduced the creation of a biomimetic sensor utilizing sarcosine-imprinted poly-aminothiophenol (p-ATP) layers applied to carbon electrodes with a gold-nanoparticle interlayer, serving as the recognition element by electropolymerization for sarcosine detection. The research results demonstrated that the sarcosine sensor developed with the MIP/AuNPs/SPCE heterostructure exhibited enhanced sensitivity relative to the traditional MIP/SPAuE electrode used for comparative analysis [47]. A study on the rapid and selective identification of sarcosine was performed by Sheydaei et al. This study involved the preparation of MIP nanobeads by a straightforward sol-gel approach, utilizing methacrylic acid as a functional monomer in a blend of acetonitrile and water as a pore forming, alongside sarcosine. Following the extraction of sarcosine from the polymeric matrix, the purified MIP was employed as a targeted altering agent for a carbon paste electrode (CPE) for the quantification of sarcosine. In this study, the critical factors such as the effect of pH on the electrochemical behavior of the designed electrodes, the effect of the modifier amount and deposition time the influence of the rate of scan on the peak currents and potentials in the sensor signals were investigated comprehensively [48]. Recently, Wong et al. discussed the creation of carbon paste electrode with ionic liquid and magnetic MIP for sensitive and selective determination of sarcosine. The researchers observed that treatment of carbon paste electrode with ionic liquid and magnetic MIP offered high catalytic activity against sarcosine oxidation and increased detectability of sarcosine in biological samples by increasing the analytical signal. The proposed approach revealed a determination range of 2×10^{-7} to 1.04×10^{-4} mol L^{-1} and a low detection limit of 5.1×10^{-8} mol L^{-1} [49]. On the other hand, levels of STEAP1, a cell surface protein of the Prostatic Six-Transmembrane Epithelial Antigens (STEAP) family whose main function is cell-to-cell communication and cell growth, elevated in malignant tissue than in normal tissue, and these concentrations are correlated with a more aggressive stage of malignancy, according to Barroca-Ferreira and colleagues [50]. A variety of sources suggest that STEAP1 is applicable for the prognosis and diagnosis of prostate cancer and presents a potential target of treatment for the disease [50–52]. Carvalho et al. created a MIP on a SPCE modified with a nanocomposite of carbon nanotubes decorated with dendritic platinum nanoparticles (CNTs-PAH/Pt) for the precise and selective detection of STEAP1. The MIPs were synthesized using the electropolymerization of a mixture of STEAP1 and the functional monomer pyrrole-2-carboxylic acid on the modified SPCE. While the physiological limit of STEAP1 remains under investigation, the researchers indicated that the biosensor created in this study shown excellent performance for selectivity, sensitivity, and repeatability for prostate cancer diagnosis [53].

3.2. PSA detection using other measurement techniques

Electrochemiluminescence (ECL) sensors possess numerous advantages, including high sensitivity, minimal background interference, controllability, and easy configuration, facilitating their extensive use in the sensitive detection of various targets such as proteins, micro RNA, and DNA. Biocompatible ECL signal probes have enabled the measurement of minimal concentrations of PSA in serum from individuals. Wang et al. have developed a dual recognition electrochemiluminescence sensor utilizing both an aptamer and a MIP for the quantification of PSA. The aptamer was self-assembled onto electrodes modified with AuNP through Au–S linkages. The MIP membrane layer was produced using the electropolymerization of dopamine. The measurement principle relies on the reduction of the ECL response of luminol in solution following the binding of PSA to the printed cavities. The "signal-off" technique has been used for PSA diagnosis, exhibiting a broad linear range and a LOD of 5 pg mL^{-1} to 50 ng mL^{-1}, with a LOD of 3 pg mL^{-1} [54].

MIPs are preferred as detection components in biosensors for effective recognition of targets, while fluorescence imaging enables highly sensitive detection and ease of use. MIP-based fluorescence detection systems have garnered interest across various domains, including chemical and biological investigation. Innovative methodologies in molecular imprinting and fluorescence detection are promising to enhance the sensing performance of MIP-based fluorescence sensors. Construction methodologies such as hierarchical architecture, including core-shell, hollow, and mesoporous architectures, post-imprinting modifications (PIM), and proportionate fluorescence have been developed to enhance the sensing properties of these sensors [55]. Saeki et al. presented a sensing strategy using MIP and a newly designed multifunctional PIM reagent (PIR) for PSA detection. PIR, which has an interaction site and dual reaction sites for PIMs, provided high signal-to-noise ratio [56].

Turan and colleagues introduced a plasmonic biosensor design for PSA detection, integrating the great selectivity of MIP with the exceptional sensitivity of SERS. Magnetic MIP nanoparticles were synthesized utilizing tannic acid (TA) as a functional monomer and employed as a "antibody-free" capture probe for PSA. TA is distinguished by its favorable solid-liquid interface characteristics, self-polymerization capabilities, and the ability to generate hydrophilic coatings owing to the abundance of hydroxyl groups. The approach mainly depends on the selectivity of magnetic MIP nanoparticles used as capture probes for PSA and the high sensitivity of SERS nanotag. The performance of the proposed method in clinical applications was tested by comparing with ELISA test and the results that were observed demonstrated that the method has sufficient accuracy and sensitivity for clinical applications [57].

Table 1 outlines the properties of MIP-based biosensor applications in the early detection of lung and prostate cancer.

4. Conclusion

MIP-based biosensors exhibit considerable potential for noninvasive diagnostic techniques and great selectivity in prostate and lung cancer. The improved identification of target biomarkers in prostate cancer elevates MIP applications within this field. The elevated specificity and stability of MIPs allow these sensors to proficiently identify target molecules, even amidst the intricacies of biological settings. Nonetheless, certain constraints of conventional polymerization methods may result in structures that inadequately detect biomarkers with precision. This scenario presents a significant impediment, particularly for the identification of biomarkers at minimal doses. Currently, interdisciplinary methodologies like nanotechnology and surface engineering has the capability to surmount these constraints. Nanoscale changes of electrode surfaces enhance signal amplification and lower detection limits [58–60]. In future decades, the use of artificial intelligence (AI) and machine learning (ML) in MIP-based biosensors can enhance

Table 1
Summary of MIP-based biosensor applications in diagnosing lung and prostate cancer.

Sensing Principle	Platform	Analyte	Determination range	Limit of Detection	Refs.
CV and EIS	MIP/GCE	GSSG, GSH, Cys, Cyss, $NADP^+$ and NADPH	10^{-11} –10^{-8} mol L^{-1}	20 pmol L^{-1}	[12]
SWV	PDA coated on Fe_3O_4 nanoparticles	CEA and AFP	0.001–5 ng mL^{-1}	CEA: 0.35 pg mL^{-1} AFP: 0.3 pg mL^{-1}	[18]
CV and EIS	DMIP/ FTO	CEA and AFP	CEA: 5–10^4 pg mL^{-1} AFP: 10 - 10^4 pg mL^{-1}	CEA: 1.6 pg mL^{-1} AFP: 3.3 pg mL^{-1}	[19]
PEC	MIP/HGNBs-$MoSe_2$/GCE	CEA	0.05 – 5 ng mL^{-1}	11.2 pg mL^{-1}	[20]
SERS	PDA encapsulated Gold coated microarray substrates	CEA	0,1 pg mL^{-1} – 10 μg mL^{-1}	0.064 pg mL^{-1}	[22]
SERS	SAM coated glass slide	CEA	1 ng mL^{-1} - 10 μg mL^{-1}	LOD: 5.56 × 10^{-14} M LOQ: 5.6 × 10^{-12} M	[23]
SWV, EIS, SERS	GSPE	CEA	1 - 1000 ng mL^{-1}	1 ng mL^{-1}	[24]
SERS	Glass slide/MIP	CEA	n/a	0.1 ng mL^{-1}	[25]
DPV	SPCE modified with PEDOT:PSS@Fc	PSA	1 × 10^{-7} – 1 × 10^{-4} ng mL^{-1}	(8.3 ± 1.3) × 10^{-8} ng mL^{-1}	[29]
DPV	GSPE	PSA	0,01 - 4,0 ng mL^{-1}	2 pg mL^{-1}	[30]
EIS	GSPE	PSA, Myo	PSA: 0.01 - 100 ng mL^{-1} Myo: 1-20,000 ng mL^{-1}	PSA: 5.4 pg mL^{-1} Myo: 0.83 ng mL^{-1}	[33]
CV	Glass cover slips	PSA	10 fg mL^{-1} – 100 ng mL^{-1}	PSA-MIP: 8 × 10^{-5} ng mL^{-1}	[36]
DPV and CV	Gold electrode	PSA	1 - 60 μg L^{-1}	1 μg L^{-1}	[38]
DPV, EIS and CV	GCE	PSA	1 × 10^{-4} - 1 × 10^4 ng mL^{-1}	0.03 pg mL^{-1}	[39]
EIS	Gold electrode	PSA	100 pg ml^{-1} - 100 ng ml^{-1}	1 pg ml^{-1}	[43]
All solid-state potentiometry	Micropipette tips	Sarcosine	10^{-5} - 10^{-8} mol L^{-1}	7.8 × 10^{-8} mol L^{-1}	[46]
EIS	AuNPs/SPCE/MIP	Sarcosine	1 ng mL^{-1} – 1.6 μg mL^{-1}	0,84 ng mL^{-1}	[47]
DPV and CV	CPE /MIP	Sarcosine	5 μM - 1.1 mM	0,38 μM	[48]
DPV and CV	CPE modified with ionic liquid and magnetic MIP	Sarcosine	2 × 10^{-7} – 1.04^{-4} mol L^{-1}	5.1 × 10^{-8} mol L^{-1}	[49]
EIS, CV and SWV	SPCE modified with CNTs-PAH/Pt	STEAP-1	130 pg ml^{-1} – 13 μg ml^{-1}	n/a	[53]
ECL	GCE modified with AuNP	PSA	5 pg mL^{-1} - 50 ng mL^{-1}	3 pg mL^{-1}	[54]
Fluorescent	Gold-coated glass substrates	PSA	5 - 150 ng mL^{-1}	2.35 ng mL^{-1}	[56]
SERS	Magnetic MIP	PSA	0,05 - 0,3 mg mL^{-1}	LOD: 0.9 pg mL^{-1} LOQ: 3.2 pg mL^{-1}	[57]

Abbreviations: CV, Cyclic voltammetry; EIS, Electrochemical impedance spectroscopy; MIP, Molecularly imprinted polymer; SWV, Square wave voltammetry; DMIP, Dual-template molecularly imprinted polymer; DPV, Differential pulse voltammetry; GCE, Glassy carbon electrodes; GSSG, Glutathione disulfide; GSH, Glutathione; Cys, Cysteine; Cyss, Cystine; $NADP^+$, β-nicotinamide adenine dinucleotide phosphate; NADPH, Nicotinamide adenine dinucleotide; PDA, Polydopamine; CEA, Carcinoembryonic antigen; AFP, α-fetoprotein; DMIP, Dual-template molecularly imprinted polymer; FTO, fluorine-doped tin oxide; PEC, Photoelectrochemical; HGNBs, Hollow gold nanospheres; MoSe2, Molybdenum diselenide; SERS, Surface-enhanced raman spectroscopy; SAM, Self-assembled monolayers; GSPE, Gold screen-printed electrode; PEDOT:PSS@Fc, polystyrenesulfonate-doped poly(3,4-ethylenedioxythiophene) ferrocene composite; SPCE, Screen-printed carbon electrode; Myo, Miyoglobin; ECL, Electrochemiluminescence; CNTs-PAH/Pt, Carbon nanotubes decorated with dendritic platinum nanoparticles.

biomarker detection processes. These technologies facilitate the analysis of polymerization processes and sensor responses, enabling sensors to yield results more rapidly and with more accuracy. The trend of creating biocompatible and ecologically sustainable MIP materials through green chemistry methods paves the way for innovative sensor design. The utilization of bio-based functional monomers and solvents can diminish environmental consequences and enhance the incorporation of sensors into biological systems.

The significance of MIP-based biosensors in cancer diagnosis is enhanced by technological and materials research breakthroughs. In the future, the development of portable and cost-effective devices may promote the extensive utilization of these technologies in therapeutic contexts. Furthermore, the advancement of sensor platforms that can identify simultaneous detection of various biomarkers enhances the comprehensiveness of early diagnostic procedures [12,18,19]. Investigations in this field will provide an essential basis for medical diagnosis and personalized medicine applications. On the other hand, significant limitations of MIP-based biosensors designed for the recognition of multiple analytes are becoming apparent. These constraints encompass reducing cross-interactions across analytes while ensuring elevated selectivity and sensitivity. Polymer matrices employed in the formulation of MIPs are typically created to target a singular analyte. Nonetheless, the necessity for the detection of multiple analytes demands the establishment of various recognition sites on a singular surface for distinct analytes. This may result in the polymer losing its homogeneity and the binding sites influencing one another. Moreover, achieving signal separation and analytical precision in multi-analyte systems becomes challenging, particularly when the physicochemical properties of the analytes are analogous. To address these restrictions, innovative polymer architectures and hybrid sensor systems are presented. Surface engineering and nanoscale editing techniques can be employed to establish distinct binding sites for various analytes. Furthermore, integrating MIPs with optical, electrochemical, or fluorescence-based sensor technologies helps mitigate cross-interaction issues by offering distinct signal readout channels for each analyte.

Over the past decade, MIPs and aptamers have demonstrated considerable advancements in molecular recognition capabilities for biochemical sensing applications . Recently, the MIP-aptamer, an innovative hybrid recognition element, integrates the benefits of both recognition components [42]. Investigations have been conducted to demonstrate the recognition strategy that incorporates MIP-aptamer as a hybrid recognition element for PSA determination, as previously mentioned [43,54]. The researchers emphasize that the selectivity and sensitivity of biosensors are enhanced by the integration of MIPs with aptamers, which is achieved through a dual recognition element approach. The chemical and thermal durability of MIPs, along with the high binding specificity of aptamers, provide a robust recognition mechanism. This method offers benefits, including the capacity to target a diverse array of analytes and minimize false positive and negative outcomes. Nonetheless, functionalizing both recognition elements on a single surface is intricate, and the synthesis procedures are laborious and expensive. The sensitivity of aptamers to environmental variables and potential cross-reactions may constrain the system's performance. Enhancing the efficacy and cost-effectiveness of these hybrid systems in the future may provide substantial advancements in biosensor applications.

The relevance of MIP-based biosensors in cancer diagnostics is bolstered by advancements in technology and materials research. In the future, the advancement of portable and affordable devices may facilitate the widespread deployment of these technologies in therapeutic settings. Furthermore, the advancement of sensor platforms that can identify many biomarkers may enhance the comprehensiveness of early diagnostic procedures. Research in this domain will establish a crucial foundation for both medical diagnostics and customized medicine applications.

CRediT authorship contribution statement

İnci Uludağ Anıl: Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Mustafa Kemal Sezgintürk:** Conceptualization, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

References

[1] F. Bray, J. Ferlay, I. Soerjomataram, R.L. Siegel, L.A. Torre, A. Jemal, Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA Cancer J. Clin. 68 (2018) 394–424, https://doi.org/10.3322/caac.21492.

[2] G. Pilvenyte, V. Ratautaite, R. Boguzaite, A. Ramanavicius, R. Viter, S. Ramanavicius, Molecularly imprinted polymers for the determination of cancer biomarkers, Int. J. Mol. Sci. 24 (2023) 4105, https://doi.org/10.3390/ijms24044105.

[3] O.I. Parisi, F. Francomano, M. Dattilo, F. Patitucci, S. Prete, F. Amone, F. Puoci, The evolution of molecular recognition: from antibodies to molecularly imprinted polymers (MIPs) as artificial counterpart, J. Funct. Biomater. 13 (2022), https://doi.org/10.3390/jfb13010012.

[4] M. Garg, N. Pamme, Strategies to remove templates from molecularly imprinted polymer (MIP) for biosensors, TrAC-Trend Anal. Chem. 170 (2024) 117437, https://doi.org/10.1016/j.trac.2023.117437.

[5] G. Ertürk, B. Mattiasson, Molecular imprinting techniques used for the preparation of biosensors, Sensors 17 (2017) 288, https://doi.org/10.3390/s17020288.

[6] G. Pilvenyte, V. Ratautaite, R. Boguzaite, S. Ramanavicius, C.F. Chen, R. Viter, A. Ramanavicius, Molecularly imprinted polymer-based electrochemical sensors for the diagnosis of infectious diseases, Biosensors. (Basel) 13 (2023) 620, https://doi.org/10.3390/bios13060620.

[7] L.M. Seijo, N. Peled, D. Ajona, M. Boeri, J.K. Field, G. Sozzi, R. Pio, J.J. Zulueta, A. Spira, P.P. Massion, P.J. Mazzone, L.M. Montuenga, Biomarkers in lung cancer screening: achievements, promises, and challenges, J. Thorac. Oncol. 14 (2019) 343–357, https://doi.org/10.1016/j.jtho.2018.11.023.

[8] L. Zhou, Y. Wang, R. Xing, J. Chen, J. Liu, W. Li, Z. Liu, Orthogonal dual molecularly imprinted polymer-based plasmonic immunosandwich assay: a double characteristic recognition strategy for specific detection of glycoproteins, Biosens. Bioelectron. 145 (2019) 111729, https://doi.org/10.1016/j.bios.2019.111729.

[9] M. Grunnet, J.B. Sorensen, Carcinoembryonic antigen (CEA) as tumor marker in lung cancer, Lung Cancer 76 (2012) 138–143, https://doi.org/10.1016/j.lungcan.2011.11.012.

[10] L. Kennedy, J.K. Sandhu, M.E. Harper, M, Cuperlovic-culf, role of glutathione in cancer: from mechanisms to therapies, Biomolecules 10 (2020) 1–27, https://doi.org/10.3390/biom10101429.

[11] H.Q. Ju, J.F. Lin, T. Tian, D. Xie, R.H. Xu, NADPH homeostasis in cancer: functions, mechanisms and therapeutic implications, Signal. Transduct. Target. Ther. 5 (2020) 231, https://doi.org/10.1038/s41392-020-00326-0.

[12] J. Liu, Y. Wang, X. Liu, Q. Yuan, Y. Zhang, Y. Li, Novel molecularly imprinted polymer (MIP) multiple sensors for endogenous redox couples determination and their applications in lung cancer diagnosis, Talanta 199 (2019) 573–580, https://doi.org/10.1016/j.talanta.2019.03.018.

[13] P.S. Sharma, A. Garcia-Cruz, M. Cieplak, K.R. Noworyta, W. Kutner, 'Gate effect' in molecularly imprinted polymers: the current state of understanding, Curr. Opin. Electrochem. 16 (2019) 50–56, https://doi.org/10.1016/j.coelec.2019.04.020.

[14] J. Wang, Y. Chu, J. Li, T. Wang, L. Sun, P. Wang, X. Fang, F. Zeng, J. Wang, F. Zeng, The clinical value of carcinoembryonic antigen for tumor metastasis assessment in lung cancer, PeerJ. 7 (2019) e7433, https://doi.org/10.7717/peerj.7433.

[15] Y.S. Kuo, M.Y. Zheng, M.F. Huang, C.C. Miao, L.H. Yang, T.W. Huang, Y.T. Chou, Association of divergent carcinoembryonic antigen patterns and lung cancer progression, Sci. Rep. 10 (2020) 2066, https://doi.org/10.1038/s41598-020-59031-1.

[16] S. Wang, L. Zhang, J. Zeng, X. Hu, X. Wang, L. Yu, D. Wang, L. Cheng, R. Ahmed, V. Romanovski, P. Li, Z. Zhang, Multi-templates molecularly imprinted polymers for simultaneous recognition of multiple targets: from academy to application, TrAC-Trend Anal. Chem. 166 (2023) 117173, https://doi.org/10.1016/j.trac.2023.117173.

[17] R. Shen, Y.C. Yu, R. Lan, Progress in application of dual/multi-template molecularly imprinted polymers, Chin. J. Anal. Chem. 49 (2021) e21205–e21215, https://doi.org/10.1016/S1872-2040(21)60118-4.

[18] D. Wang, N. Gan, H. Zhang, T. Li, L. Qiao, Y. Cao, X. Su, S. Jiang, Simultaneous electrochemical immunoassay using graphene-Au grafted recombinant apoferritin-encoded metallic labels as signal tags and dual-template magnetic molecular imprinted polymer as capture probes, Biosens. Bioelectron. 65 (2015) 78–82, https://doi.org/10.1016/j.bios.2014.09.085.

[19] N. Taheri, H. Khoshsafar, M. Ghanei, A. Ghazvini, H. Bagheri, Dual-template rectangular nanotube molecularly imprinted polypyrrole for label-free impedimetric sensing of AFP and CEA as lung cancer biomarkers, Talanta 239 (2022) 123146, https://doi.org/10.1016/j.talanta.2021.123146.

[20] C. Wang, Y. Wang, H. Zhang, H. Deng, X. Xiong, C. Li, W. Li, Molecularly imprinted photoelectrochemical sensor for carcinoembryonic antigen based on polymerized ionic liquid hydrogel and hollow gold nanoballs/MoSe2 nanosheets, Anal. Chim. Acta 1090 (2019) 64–71, https://doi.org/10.1016/j.aca.2019.09.029.

[21] T.J. Moore, A.S. Moody, T.D. Payne, G.M. Sarabia, A.R. Daniel, B. Sharma, In vitro and in vivo sers biosensing for disease diagnosis, Biosensors. (Basel) 8 (2018) 46, https://doi.org/10.3390/bios8020046.

[22] X. Lin, Y. Wang, L. Wang, Y. Lu, J. Li, D. Lu, T. Zhou, Z. Huang, J. Huang, H. Huang, S. Qiu, R. Chen, D. Lin, S. Feng, Interference-free and high precision biosensor based on surface enhanced Raman spectroscopy integrated with surface molecularly imprinted polymer technology for tumor biomarker detection in human blood, Biosens. Bioelectron. 143 (2019) 111599, https://doi.org/10.1016/j.bios.2019.111599.

[23] L. Zhou, Y. Wang, R. Xing, J. Chen, J. Liu, W. Li, Z. Liu, Orthogonal dual molecularly imprinted polymer-based plasmonic immunosandwich assay: a double characteristic recognition strategy for specific detection of glycoproteins, Biosens. Bioelectron. 145 (2019) 111729, https://doi.org/10.1016/j.bios.2019.111729.

[24] M.C.C.G. Carneiro, A. Sousa-Castillo, M.A. Correa-Duarte, M.G.F. Sales, Dual biorecognition by combining molecularly-imprinted polymer and antibody in SERS detection. Application to carcinoembryonic antigen, Biosens. Bioelectron. 146 (2019) 111761, https://doi.org/10.1016/j.bios.2019.111761.

[25] J. Feng, X. Li, H. Cheng, W. Huang, H. Kong, Y. Li, L. Li, A boronate-modified molecularly imprinted polymer labeled with a SERS-tag for use in an antibody-free immunoassay for the carcinoembryonic antigen, Mikrochim. Acta 186 (2019) 1–9, https://doi.org/10.1007/s00604-019-3972-x.

[26] M. Adamaki, V. Zoumpourlis, Prostate cancer biomarkers: from diagnosis to prognosis and precision-guided therapeutics, Pharmacol. Ther. 228 (2021) 107932, https://doi.org/10.1016/j.pharmthera.2021.107932.

[27] S. Ramanavicius, A. Jagminas, A. Ramanavicius, Advances in molecularly imprinted polymers based affinity sensors, Polymers. (Basel) 13 (2021) 974, https://doi.org/10.3390/polym13060974.

[28] M.B. Regasa, T.R. Soreta, O.E. Femi, P.C. Ramamurthy, S. Subbiahraj, Novel multifunctional molecular recognition elements based on molecularly imprinted poly (aniline-co-itaconic acid) composite thin film for melamine electrochemical detection, Sens. Biosens. Res. 27 (2020) 100318, https://doi.org/10.1016/j.sbsr.2019.100318.

[29] S. Khumngern, P. Thavarungkul, P. Kanatharana, T. Bejrananda, A. Numnuam, Molecularly imprinted electrochemical sensor based on poly(o-phenylenediamine-co-o-aminophenol) incorporated with poly(styrenesulfonate) doped poly(3,4-ethylenedioxythiophene) ferrocene composite modified screen-printed carbon electrode for highly sensitive and selective detection of prostate cancer biomarker, Microchem. J. 177 (2022) 107311, https://doi.org/10.1016/j.microc.2022.107311.

[30] Z. Yazdani, H. Yadegari, H. Heli, A molecularly imprinted electrochemical nanobiosensor for prostate specific antigen determination, Anal. Biochem. 566 (2019) 116–125, https://doi.org/10.1016/j.ab.2018.11.020.

[31] I.E. Elkholi, M.E. Elsherbiny, M. Emara, Myoglobin: from physiological roles to potential implications in cancer, Biochim. Biophys. Acta Rev. Cancer 1877 (2022) 188706, https://doi.org/10.1016/j.bbcan.2022.188706.

[32] G.B. Postnikova, E.A. Shekhovtsova, Myoglobin expression by tumor cells and its role in progression of malignancy, Biochem. (Mosc) Suppl. Ser. A Membr. Cell Biol. 18 (2024) 285–295, https://doi.org/10.1134/S1990747824700284.

[33] P. Karami, H. Bagheri, M. Johari-Ahar, H. Khoshsafar, F. Arduini, A. Afkhami, Dual-modality impedimetric immunosensor for early detection of prostate-specific antigen and myoglobin markers based on antibody-molecularly imprinted polymer, Talanta 202 (2019) 111–122, https://doi.org/10.1016/j.talanta.2019.04.061.

[34] Y. Ma, X.L. Shen, Q. Zeng, L.S. Wang, A glassy carbon electrode modified with graphene nanoplatelets, gold nanoparticles and chitosan, and coated with a molecularly imprinted polymer for highly sensitive determination of prostate specific antigen, Mikrochim. Acta 184 (2017) 4469–4476, https://doi.org/10.1007/s00604-017-2458-y.

[35] S.K. Vashist, J.H.T. Luong, Recent advances in electrochemical biosensing schemes using graphene and graphene-based nanocomposites, Carbon. N. Y. 84 (2015) 519–550, https://doi.org/10.1016/j.carbon.2014.12.052.

[36] G. Ertürk, M. Hedström, M.A. Tümer, A. Denizli, B. Mattiasson, Real-time prostate-specific antigen detection with prostate-specific antigen imprinted capacitive biosensors, Anal. Chim. Acta 891 (2015) 120–129, https://doi.org/10.1016/j.aca.2015.07.055.
[37] G. Ertürk, B. Mattiasson, Capacitive biosensors and molecularly imprinted electrodes, Sensors (Switzerland) 17 (2017) 390, https://doi.org/10.3390/s17020390.
[38] L. Abbasy, A. Mohammadzadeh, M. Hasanzadeh, N. Razmi, Development of a reliable bioanalytical method based on prostate specific antigen trapping on the cavity of molecular imprinted polymer towards sensing of PSA using binding affinity of PSA-MIP receptor: a novel biosensor, J. Pharm. Biomed. Anal. 188 (2020) 113447, https://doi.org/10.1016/j.jpba.2020.113447.
[39] G. Zhang, Y. Yu, L. Zhang, B. Lin, Y. Wang, M. Guo, Y. Cao, Precise detection of prostate specific antigen in serum: a surface molecular imprinted sensor based on novel cooperated signal amplification strategy, Sens. Actuators B Chem. 302 (2020) 126998, https://doi.org/10.1016/j.snb.2019.126998.
[40] S. Dietl, H. Sobek, B. Mizaikoff, Epitope-imprinted polymers for biomacromolecules: recent strategies, future challenges and selected applications, TrAC-Trend Anal. Chem. 143 (2021) 116414, https://doi.org/10.1016/j.trac.2021.116414.
[41] H. Shao, L. Zhao, Z. Liu, J. Li, An epitope imprinted electrochemical sensor for highly sensitive and selective determination of prostate-specific antigen, Mikrochim. Acta 191 (2024) 660, https://doi.org/10.1007/s00604-024-06737-y.
[42] G.K. Ali, K.M. Omer, Molecular imprinted polymer combined with aptamer (MIP-aptamer) as a hybrid dual recognition element for bio(chemical) sensing applications, Review, Talanta 236 (2022) 122878, https://doi.org/10.1016/j.talanta.2021.122878.
[43] P. Jolly, V. Tamboli, R.L. Harniman, P. Estrela, C.J. Allender, J.L. Bowen, Aptamer-MIP hybrid receptor for highly sensitive electrochemical detection of prostate specific antigen, Biosens. Bioelectron. 75 (2016) 188–195, https://doi.org/10.1016/j.bios.2015.08.043.
[44] A.R. Lima, M. de L. Bastos, M. Carvalho, P. Guedes de Pinho, Biomarker discovery in human prostate cancer: an update in metabolomics studies, Transl. Oncol. 9 (2016) 357–370, https://doi.org/10.1016/j.tranon.2016.05.004.
[45] A. Sreekumar, L.M. Poisson, T.M. Rajendiran, A.P. Khan, Q. Cao, J. Yu, B. Laxman, R. Mehra, R.J. Lonigro, Y. Li, M.K. Nyati, A. Ahsan, S. Kalyana-Sundaram, B. Han, X. Cao, J. Byun, G.S. Omenn, D. Ghosh, S. Pennathur, D.C. Alexander, A. Berger, J. R. Shuster, J.T. Wei, S. Varambally, C. Beecher, A.M. Chinnaiyan, Metabolomic profiles delineate potential role for sarcosine in prostate cancer progression, Nature 457 (2009) 910–914, https://doi.org/10.1038/nature07762.
[46] S. Fernández-Puig, A.R. Lazo-Fraga, B.A. Korgel, G. Oza, A. Dutt, V. Vallejo-Becerra, A.C. Valdés-González, A.U. Chávez-Ramírez, Molecularly imprinted polymer-silica nanocomposite based potentiometric sensor for early prostate cancer detection, Mater. Lett. 309 (2022) 131324, https://doi.org/10.1016/j.matlet.2021.131324.
[47] T.P. Nguy, T. Van Phi, D.T.N. Tram, K. Eersels, P. Wagner, T.T.N. Lien, Development of an impedimetric sensor for the label-free detection of the amino acid sarcosine with molecularly imprinted polymer receptors, Sens. Actuators B Chem. 246 (2017) 461–470, https://doi.org/10.1016/j.snb.2017.02.101.
[48] O. Sheydaei, H. Khajehsharifi, H.R. Rajabi, Rapid and selective diagnose of sarcosine in urine samples as prostate cancer biomarker by mesoporous imprinted polymeric nanobeads modified electrode, Sens. Actuators B Chem. 309 (2020) 127559, https://doi.org/10.1016/j.snb.2019.127559.
[49] A. Wong, S. Zeb, A.M. Santos, M.H.A. Feitosa, S. Khan, F.C. Moraes, M.D.P. T. Sotomayor, Detection of prostate cancer using an electrochemical sensor integrated with molecular imprinting technology and ionic liquid: a novel approach, J. Solid. State Electrochem. (2024) 1–10, https://doi.org/10.1007/s10008-024-05855-0.
[50] S.R. Bott, K.L. Ng (Eds.), Prostate Cancer, Exon Publications, 2021, https://doi.org/10.36255/exonpublications.prostatecancer.2021.
[51] J. Moreaux, A. Kassambara, D. Hose, B. Klein, STEAP1 is overexpressed in cancers: a promising therapeutic target, Biochem. Biophys. Res. Commun. 429 (2012) 148–155, https://doi.org/10.1016/j.bbrc.2012.10.123.
[52] K. Khanna, N. Salmond, K.S. Lynn, H.S. Leong, K.C. Williams, Clinical significance of STEAP1 extracellular vesicles in prostate cancer, Prostate Cancer Prostatic. Dis. 24 (2021) 802–811, https://doi.org/10.1038/s41391-021-00319-2.
[53] M. Carvalho, R.M. Gomes, S.M. Rocha, J. Barroca-Ferreira, C.J. Maia, L. Guillade, M.A. Correa-Duarte, L.A. Passarinha, F.T.C. Moreira, Development of a novel electrochemical biosensor based on plastic antibodies for detection of STEAP1 biomarker in cancer, Bioelectrochemistry 152 (2023) 108461, https://doi.org/10.1016/j.bioelechem.2023.108461.
[54] Y. Wang, X. Kan, Sensitive and selective "signal-off" electrochemiluminescence sensing of prostate-specific antigen based on an aptamer and molecularly imprinted polymer, Analyst 146 (2021) 7693–7701, https://doi.org/10.1039/d1an01645h.
[55] Q. Yang, J. Li, X. Wang, H. Peng, H. Xiong, L. Chen, Strategies of molecular imprinting-based fluorescence sensors for chemical and biological analysis, Biosens. Bioelectron. 112 (2018) 54–71, https://doi.org/10.1016/j.bios.2018.04.028.
[56] T. Saeki, E. Takano, H. Sunayama, Y. Kamon, R. Horikawa, Y. Kitayama, T. Takeuchi, Signalling molecular recognition nanocavities with multiple functional groups prepared by molecular imprinting and sequential post-imprinting modifications for prostate cancer biomarker glycoprotein detection, J. Mater. Chem. B 8 (2020) 7987–7993, https://doi.org/10.1039/d0tb00685h.
[57] E. Turan, A. Zengin, Z. Suludere, N.Ö. Kalkan, U. Tamer, Construction of a sensitive and selective plasmonic biosensor for prostate specific antigen by combining magnetic molecularly-imprinted polymer and surface-enhanced Raman spectroscopy, Talanta 237 (2022) 122926, https://doi.org/10.1016/j.talanta.2021.122926.
[58] X. Dong, C. Zhang, X. Du, Z. Zhang, Recent advances of nanomaterials-based molecularly imprinted electrochemical sensors, Nanomaterials 12 (2022) 1913, https://doi.org/10.3390/nano12111913.
[59] C. Zhong, B. Yang, X. Jiang, J. Li, Current progress of nanomaterials in molecularly imprinted electrochemical sensing, Crit. Rev. Anal. Chem. 48 (2018) 15–32, https://doi.org/10.1080/10408347.2017.1360762.
[60] A.A. Lahcen, A. Amine, Recent advances in electrochemical sensors based on molecularly imprinted polymers and nanomaterials, Electroanalysis 31 (2019) 188–201, https://doi.org/10.1002/elan.201800623.